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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,285	03/02/2005	Nitin Bhalachandra Dharmadhikari	006420.00004	4683

22508 7590 12/07/2009

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EXAMINER	
SIMMONS, CHRIS E	
ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
12/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,285	DHARMADHIKARI ET AL.	
	Examiner	Art Unit	
	CHRIS E. SIMMONS	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,10,11,14-18,23 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7,10,11,14-18,23 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 06/03/2009, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Response to Arguments

Applicant's arguments, see page 7, lines 14-20, filed 06/03/2009, with respect to support for a "greater rate and extent of absorption" have been fully considered and are persuasive. The new matter rejection of 03/18/2009 has been withdrawn.

Claim Rejections - 35 USC § 103

The two rejections will be discussed together infra, considering the issues for both are essentially the same.

Claims 1, 7, 10, 11, 14-18, 23 and 31 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Liversidge et al. (US 5,145,684) in view of Scaife et al. (US 6,407,128).

Claims 1, 7, 10, 11, 14-18, 23 and 31 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Martin et al. (US 4,344,934) in view of Scaife et al. (US 6,407,128).

At bottom of page 9, applicant argues that Scaife teaches that when its composition is given to a patient with food, the extent of absorption increases, but the rate of absorption decreases.

Applicant has submitted a Declaration regarding a communication by Michael Scaife, allegedly the named inventor of the Scaife reference, to the FDA, along with a study that concluded that the data therein "provides compelling evidence that *in vitro* dissolution cannot be used as a surrogate of *in vivo* performance for pharmaceutical equivalents of Skelaxin". This is not found to be persuasive because the Scaife reference is not limited to *in vitro* dissolution. The Scaife reference discloses bioavailabilty data for tests performed in male and female subjects as well; the primary Liveridge reference also discloses bioavailability data for test performed in dogs. Accordingly, the Declaration with regard to limitations of *in vitro* dissolution being used as a surrogate of *in vivo* performance appears to not be relevant; and applicant's arguments regarding the lack of predictive value for *in vitro* Skelaxin dissolution for *in vivo* Skelaxin performance are not persuasive.

At page 11, applicant's arguments rely on *The Proctor & Gamble Co. v. Teva Pharm, USA, Inc.* (Fed. Cir. May 13, 2009) (holding the claimed invention to be non-obvious). In *Proctor & Gamble*, the Federal Circuit noted that the patent owner' experts testified that a person having ordinary skill, at the time of invention, "realized that the properties of bisphosphonates could not be anticipated based on their structure". The Federal Circuit also noted that the preeminent authority on bisphosphonates who wrote

that "every compound, while remaining a bisphosphonates, exhibits its own physical-chemical, biological and therapeutic characteristics, so that each bisphosphonate has to be considered on its own merits...". Applicant argues that similarly, in the present case, a preeminent authority on metaxalone (active agent in Skelaxin®) indicated that every form of metaxalone exhibits its own physical-chemical, biological and therapeutic characteristics, so that each metaxalone has to be considered on its own. The examiner does not find the equivalence between the instant case and *Proctor & Gamble*. Particularly, the preeminent authority in the case law was comparing 2 completely *different* compounds (i.e., bisphosphonate isomers), while in the present case, the exact *same* compound (i.e., metaxalone) is at issue, where the difference is particle sizes. Furthermore, it has not been made clear what preeminent authority in the present case indicated that "*every form* of metaxalone exhibits its own physical-chemical, biological and therapeutic characteristics, so that each form of metaxalone has to be considered on its own". Additionally, as outlined above, assuming the Scaife inventor did indicate that *in vitro* dissolution cannot be used as a surrogate for *in vivo* bioavailabilty performance, it would appear that this indication is irrelevant because the Scaife reference of record does included *in vivo* bioavailability performance data.

Further relying on *Proctor & Gamble* at bottom of page 11 of the current response, applicant asserts that the skilled artisan was not faced with a finite number of identified, predictable solutions to the problem of increasing both the rate and extent of absorption of metaxalone. Examiner disagrees with this assertion. The primary

reference provides the skilled artisan with the knowledge to increase bioavailabilty (i.e., rate and extent of absorption) by decreasing the particle size parameter.

Applicant argues, at page 12, that one of ordinary skill in the art having the benefit of Scaife's "food" solution would not have been motivated at the time of the present invention to go in the opposite direction from Scaife's expressed teaching to administer the Scaife composition with food. The examiner disagrees with the notion that the primary references direct the skilled artisan "in the opposite direction from Scaife's expressed teaching to administer the Scaife composition with food". Both primary references disclose methods to make therapeutic compositions having increased bioavailability of therapeutic agents while Scaife provides methods of increasing the bioavailability of metaxalone. There is no conflict as suggested by applicant between these disclosures. The examiner further notes that the instant claims are product claims, not method claims; therefore, arguments regarding specific method steps such as when the composition is administered are not found to be persuasive.

At pages 14-16, applicant alleges that arguments regarding the pharmacokinetics of metaxalone in the secondary reference have been ignored or not responded to and makes arguments regarding the Tmax, Cmax and AUC. Again the examiner submits that these arguments are not persuasive and does not support the claim of unexpected results. Applicant's arguments that focus on the pharmacokinetic properties in the secondary reference alleging it shows that the reference did not result in an increase in

both rate and extent of absorption would appear to be irrelevant because the pharmacokinetic data in Table IIb at col. 5 of the reference is a pharmacokinetic comparison between the absorption of Skelaxin® when it is taken with food and the absorption of Skelaxin® when it is taken without food, whereas, applicant's pharmacokinetic data is a comparison between Skelaxin® and a different composition both taken without food. Whether applicant has increased both rate and extent of absorption of metaxalone or not does not demonstrate any unexpected results. There is no evidence provided that shows that one of ordinary skill in the art would not expect both rate and extent of absorption of metaxalone to increase when provided to the *same group* of subjects, i.e., those without food.

Applicant's attempt to create a nexus between the pharmacokinetic data in the instant case (e.g., Tmax of 2 different compositions to 1 subject population) to the pharmacokinetic data of the reference (e.g., Tmax of the same composition to 2 different subject populations - those with and those without food) to allege unexpected results is not found to be persuasive. Arguments concerning Tmax, Cmax, AUC, elimination, etc. are based on an erroneous nexus between the pharmacokinetic comparisons made in the reference and those made in the instant case.

At page 14, Applicant alleges examiner did not respond to applicant's argument that there was no reasonable expectation that both rate and extent of absorption of metaxalone would increase when given on an empty stomach. Examiner disagrees and reiterates that the primary reference discloses ways to increase the bioavailability (i.e., rate and extent of absorption) of a wide variety of active agents that would be expected

to benefit from increased solubility and bioavailability. The secondary reference is directed to increasing the bioavailability (i.e., rate and extent of absorption) of the hydrophobic compound, metaxalone; suggesting some benefit from increasing these properties. One would reasonably expect to increase the bioavailability of Skelaxin® by using it in the methods described in the primary references for increasing bioavailability.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRIS E. SIMMONS whose telephone number is

(571)272-9065. The examiner can normally be reached on Monday - Friday from 7:30 - 5:00 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/C. E. S./
Examiner, Art Unit 1612
/Gollamudi S Kishore/
Primary Examiner, Art Unit 1612